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Investigation of the change of fluoroquinolone resistance over years in urinary Escherichia coli isolates

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Abstract

Aim: In the face of rapidly increasing antibiotic resistance among urinary Escherichia coli (E.coli) isolates, it is important to follow the own resistance rates off all centers. This study aimed to investigate the resistance rates of urinary E.coli isolates against fluoroquinolones, the changes in rates over the last 6 years, and correlation with resistance rates to other antibiotics in our hospital.

Material and Methods: Antibiotic susceptibilities of urinary E.coli isolates between January 2003 and December 2008 in the Clinical Microbiology Laboratory of Dr. Lütfi Kırdar Kartal Training and Research Hospital were evaluated retrospectively. The first isolate from each patient was taken into the study.

Results: Of 5543 isolates, 27% were resistant to ciprofloxacin, 26.5 % to ofloxacin, 21.4% to gentamicin, 15.4 % to amikacin and 11.9 % produced extended spectrum beta-lactamase (ESBL). The resistance rates of ciprofloxacin and ofloxacin were 22.1% and 21.6% in 2003 and 34.3% and 35.5% in 2007, respectively (for both, $p<0.001$). ESBL rate was 4.3% in 2003 and 19% in 2008 ($p<0.001$). Of the isolates resistant to ofloxacin and ciprofloxacin, 31% and 32%, respectively, produced ESBL. There were positive correlations between fluoroquinolone resistance to other antibiotics. The resistance rates of the outpatient clinics were significantly lower than the rates of the inpatient clinics ($p<0.001$).

Discussion: The resistance rate to quinolone group antibiotics in E.coli strains isolated in various centers in our country is up to 35%, and resistance rates were generally found to be similar among quinolones. In our study, resistance to ofloxacin was found at a rate of 26.5% and ciprofloxacin resistance at a rate of 27% for E.coli strains, and no significant difference was found between them ($p<0.05$). When infections caused by bacteria with and without ESBL growth are compared in terms of mortality, morbidity and health costs, excluding the patient group in which carbapenems are used as the first treatment, in infections with ESBL-producing isolates, it has been shown that mortality is higher, length of hospital stay is longer and health costs are higher. The mortality rate in infections developed by ESBL-producing bacteria, especially in intensive care patients, varies between 30-50%.

Keywords
E.coli, Fluoroquinolone, Resistance

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Introduction

Urinary tract infections take first place among community or hospital-acquired infections, especially in children, women and the elderly. In many studies, Escherichia coli has been shown to be the most common isolated agent in urinary tract infections, ranging from 41% to 80% [1,2]. Similarly, in clinical studies in our country, the most common factor isolated is E.coli, and its frequency varies between 24% and 76% [3,4]. In the treatment of urinary system infections, fluoroquinolones have been the first preferred antibacterial drugs due to their effectiveness against most uropathogenic microorganisms and their pharmacokinetic properties [5]. Due to the widespread use of quinolones, an increase in the resistance rates of uropathogenic E.coli isolates has been reported.

Material and Methods

In our study, between January 2003 and December 2008, the results of the urine materials sent for culture to the Clinical Microbiology Laboratory of Dr. Lütfi Kırdar Training and Research Hospital, were evaluated retrospectively. E.coli isolated urine materials were taken into consideration, the data and colony numbers of isolates of these materials were examined. In this context, 5543 E.coli isolates were included in our study. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. All patients signed a free and informed consent form.

Statistics

Chi-square (x2) test and Fisher's exact probability test were used to analyze the change in antibiotic resistance rates by years and to compare the resistance rates of patients from different groups statistically ($p<0.05$). Values were considered statistically significant. SSPS 11.5 statistical program was used for all analyses.

Results

Over a 6-year-period, 5543 E.coli isolates isolated as uropathogens in the microbiology laboratory of our hospital were included in the study. Of all isolates, 3503 (63.2%) were isolated from urine materials from outpatient clinics and 1510 (27.2%) from services; 1595 (28.8%) of the isolates were isolated from urine materials from pediatric outpatient clinics and services; 43.5% of the isolates showed resistance to ampicillin-sulbactam, 34.4% to cefuroxime, 35% to cefazolin, 27% to ciprofloxacin, 26.5% to ofloxacin, 24.5% to piperacillin-tazobactam, 21.4% to gentamicin, 19% to cefepime, 18% to ceftriaxone, 15.4% to amikacin, 13.5% to cefoperazone-sulbactam, 1.2% to imipenem, 1% to meropenem, 42.1% to trimethoprim-sulfamethoxazole (Figure 1).

When the distribution of resistance development of isolates against ciprofloxacin and ofloxacin was analyzed according to years, significant differences were found in the rate of resistance development. The resistance rates were determined as 22.1% and 21.6% for ofloxacin and ciprofloxacin in 2003, respectively; In 2007, it was seen that it increased to 34.3% and 35.5%, respectively. When the resistance rates between consecutive years were compared, statistically significant differences were found between the resistance rates since 2005 ($p=0.030$, $p<0.001$ and $p=0.008$, respectively) (Figure 2).

It was observed that 11.9% of the isolates produced extended spectrum beta-lactamases (ESBL). When the distribution of ESBL producing E.coli strains according to years is examined; the rates have increased over the years; The rate, which was determined as 4.3% in 2003, increased to 19% in 2008. Statistically significant differences were found in ESBL rates by year. There were significant differences in ESBL rates between 2005 and 2006 (10.1%) and between 2006 and 2007 (19.8%) ($p=0.001$, $p=0.001$, $p<0.001$, respectively).

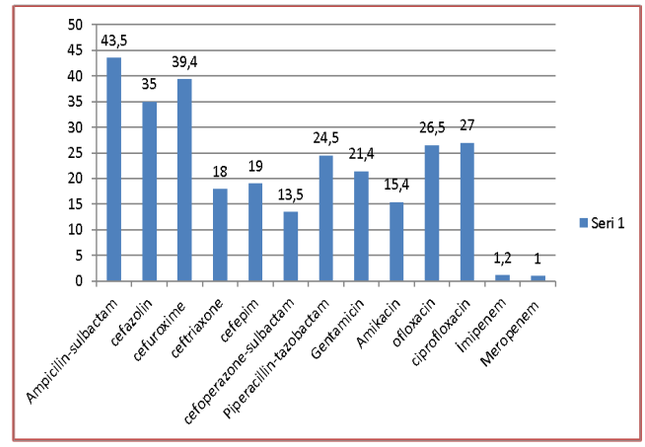

Figure 1. Antibiotic resistance rates in uropathogenic E.coli isolates (%).

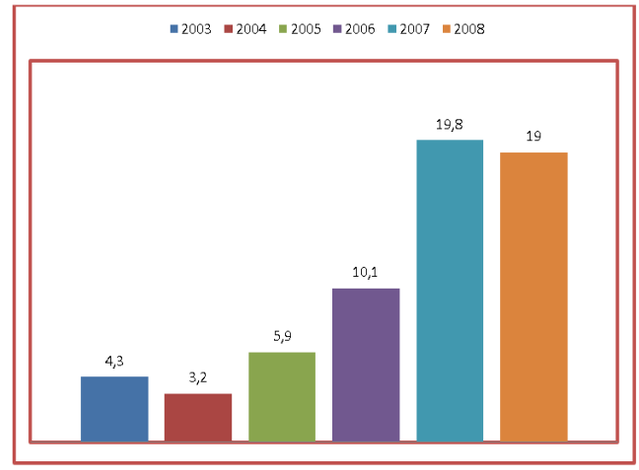

Figure 2. Distribution of non-quinolone antibiotic resistance rates of isolates by years (%).

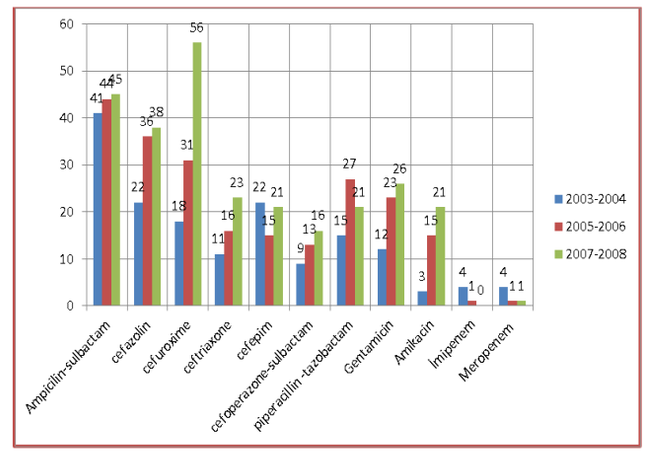

Figure 3. ESBL production rates of E.coli isolates by years (%).

Resistance of isolates to fluoroquinolones and ESBL production rates were investigated. It was observed that 31% of ofloxacin-resistant isolates and 32% of ciprofloxacin-resistant isolates produced ESBL. It was observed that only 4% of ofloxanin and ciprofloxacin-sensitive isolates produced ESBL. A statistically significant similarity was detected. While 9.5% of 1595 isolates isolated from urine samples from pediatric outpatient clinics and wards produced ESBL, 12.9% of 3948 isolates isolated from samples from other clinics were observed to produce ESBL. It was observed that there is a significant difference between them. Ofloxacin resistance was found in 8.9% of the pediatric patient group and 33.5% of the adult patient group. Ciprofloxacin-resistance was found in 10.2% of the pediatric patient group and 33.8% in the adult patient group (Figure 3).

The resistance rates of the isolates of urine samples from different polyclinics and services of our hospital were compared. As the most obvious difference, Cefepime-resistance was detected at a rate of 14.2% in the outpatient group and 34.8% in the inpatient group. While the rate of ESBL producing isolates in the outpatient group was 1.3%, it was 16.8% in the inpatient group.

Discussion

The resistance rate to quinolone group antibiotics in E.coli strains isolated in various centers in our country is up to 35%, and resistance rates among quinolones were generally found to be similar.

In a study by Leblecioğlu et al. in 2003, ampicillin resistance was found to be 23.9%, ceftriaxone resistance was 24.6% and quinolone resistance was 8.2% in uropathogenic E.coli isolates [6].

In our study, resistance to ofloxacin was found at a rate of 26.5% and ciprofloxacin resistance at a rate of 27% for E.coli strains, and no significant difference was found between them ($p<0.05$).

In a study by Zhanel et al. on outpatients, they reported ciprofloxacin resistance as 1.8%. In a study conducted by Öztürk et al. in 2008 on outpatient and service patients, they reported that ciprofloxacin resistance was 70% in hospitalized patients and 38% in outpatients [7,8]. It has been reported that resistance to norfloxacin develops in 73% of hospitalized patients and 45% of outpatients, and resistance to levofloxacin develops in 70% of hospitalized patients and 45% in outpatients.

In a study by Gonzalez et al., Ciprofloxacin resistance was found to be 24%, norfloxacin resistance was 25%, and nalidixic acid resistance was 41% in E.coli isolates. Şamlı et al. in a study they conducted in 2003 on 117 uropathogenic E.coli isolates, reported ciprofloxacin resistance as 30% and norfloxacin resistance as 58%. In our study, ciprofloxacin resistance was found to be 27% and ofloxacin resistance was found to be 27% in E. coli isolates. The rates we found are compatible with the literature. In a study by Cetin et al., ESBL was detected at a rate of 15.8% in E.coli isolates that were detected as a hospital infection. In a study by Özsoy et al. ESBL was found at a rate of 8.7% [9,10,11].

Gürdoğan et al. reported ESBL growth of 9% in hospital isolates and 7.8% in outpatient isolates, while Tünger et al. reported 13.4% growth in hospital isolates and 6.7% in non-hospital isolates. In our study, we found uropathogenic E.coli isolates producing 11.9% of ESBL in the 6 year period between 2003 and 2008 [12].

When infections caused by bacteria with and without ESBL growth are compared in terms of mortality, morbidity and health costs, excluding the patient group in which carbapenems are used as the first treatment, in infections with ESBL producing isolates, mortality has been shown to be higher, length of hospital stay longer and health costs higher. Mortality rate in infections developed by ESBL-producing bacteria, especially in intensive care patients, varies between 30-50%. It has been noted that in the case of inappropriate use of antibiotics, this rate will increase even more [13]. In particular, the close relationship between ESBL resistance and quinolone resistance makes restriction in the use of quinolones more important. Multiple resistance development is defined as the development of resistance to 3 or more different classes of antimicrobial agents.

In a study conducted to determine the resistant phenotypes of gram-negative bacteria, isolated as urinary tract infection agents, it was determined that 17.7% of E.coli isolates developed multiple resistance [14].

In a surveillance study conducted in the USA, the frequency of uropathogenic E.coli developing multiple resistance and the characteristics of infected patients were examined. 7.1% of E.coli isolates were found resistant to three or more antimicrobial drugs and were accepted as multiresistant. 97.8% of these isolates were resistant to amoxicillin, 92.8% to cotrimoxazole, 86.6% to cefazolin, 38.8% to ciprofloxacin.

Conclusion

In our study, 5543 uropathogenic E.coli isolates developed resistance to all antibiotics at certain rates. Resistance development was observed in ampicillin-sulbactam (43.5%), cefuroxime (39.4%), cefazolin (35%), ceftriaxone (18%), from aminoglycosides, 21.4% to gentamicin and 15.4% to amikacin.

In the face of increasing antibiotic resistance, especially in preventing the development of resistance against fluoroquinolones seen in uropathogenic E.coli isolates, preventing unnecessary and inappropriate antibiotic use, monitoring of regional antibiotic sensitivities and planning empirical treatments in the light of these data are essential and have vital importance.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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